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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,791	02/08/2001	Jon A. Wolff	Mirus.006.03	6737

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MIRUS CORPORATION
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EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/779,791

Applicant(s)

WOLFF ET AL

Examiner

Joseph T. Woitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This application filed February 8, 2001, is a continuation in part of application 09/312,351, filed May 14, 1999.

Applicants' amendment filed January 17, 2005, has been received and entered. The specification has been amended. Claims 7-12 have been canceled. Claim 1 has been amended. Claims 1-6 and 13 are pending and currently under examination.

Election/Restriction

As noted in previous office actions, Groups I and II (claims 1-6 and 13) had been rejoined. Applicant timely traversed the restriction (election) requirement in Paper No. 15. Claims 1-6 and 13 are currently under examination as they are drawn to a compound for inserting into an organism comprising (a) a disulfide bond which is cleaved more rapidly than oxidized glutathione and which one of the constituent thiols has a lower pKa than glutathione and (b) a transduction signal wherein the signal is a polymer containing a cationic charge.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC 112

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, the recitation of "enhances retention of said molecule inside said cell" is considered new matter.

Initially, it is noted that the basis of the previous rejection has been obviated by the above amendment. Applicants have pointed to pages 25-26 and Example 10 for support of the instant amendment.

As noted above at issue is the ability of the compound as a whole to enhances retention once the composition is across the membrane. Pages 25-26 provide guidance for contemplated retention signals, and Example 10 (pages 38-39) provides one example where a TAT conjugated fluorophore was tested by pulse chase experiments. At each of the cited portions of the specification there is no literal support for the claimed activity. It is noted that Example 10 provides a comparison of other covalent linkages and that under specific conditions reveals that a fluorophore is detected for a longer period of time when it is provided to the cell as an activated disulfide 4-aminophenyl disulphide, however provides no specific basis or discussion on the importance of the specific bond or the claimed functional bond in general for providing a

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enhanced retention. Given the evidence of record, it is unclear if the fluorophore was administered directly into the cell, i.e. without a transduction signal, if the retention would be enhanced relative to the specific example provided in the citation. The basis of the rejection focuses on the fact that the specification provides no literal support for the claimed amendment, nor any general guidance to access the instantly claimed enhanced retention of the delivered molecule. There is no guidance in the instant specification to what the artisan is required to access/test to determine whether the retention is enhanced. Moreover, beyond the specific example of the claimed compound, the specific compounds compared to this and the specific conditions that were tested in Example 10, it is unclear the single example would extend to the breadth encompassed by the instant claims. For example, in the previous office action it was noted that VP22 do not necessarily enhance deposition of a compound in the cytoplasm, however Normand *et al.* (JBC, 2001) clearly demonstrate that oligonucleotides linked to VP22 accumulate in the nuclei (bridging first and second columns, page 15042, and top of first column, page 15048). In this case, what comparison would be made, and since the molecule clearly accumulated in the cell would providing the oligo in a -SS- bond make it be retained to a greater extent?

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1-6 and 13 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As discussed above, by way of example Normand *et al.* demonstrate that

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the function of VP22, one of the specifically claimed species does not necessarily result in enhancing retention by the cell demonstrating indicating an empirical nature of testing each particular composition encompassed by the claims to determine if each structure meets the functional limitations set forth in the claims. Moreover, as discussed above, the specification fails to provide any guidance to the specific compounds or means that the "enhancement" should be assayed to determine the metes and bounds of the claims.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(f) he did not himself invent the subject matter sought to be patented.

Claims 1-6 and 13 rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter is withdrawn.

Applicants note that the invention of 6,429,200 while encompassing disulfide bonds is materially different from the instantly claimed invention. Upon review of the claims and specification of '200 and the instant specification, Examiner agrees that the claimed inventions containing disulfide bonds are different. Absence evidence to the contrary, the Inventors set forth for '200 and the instant application are believed to be correct.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Lee *et al.* Bioconjugate Chem 2001 12 :995-999.

Moulton *et al.* Drug Discovery Today 9(20):870.

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Each provide further evidence that chemically linking molecules to proteins such as TAT allow for better *in vivo* uptake of molecules.

Kang *et al.* Drug Metab Dispos. 1995 Jan;23(1):55-9 Pharmacokinetics and organ clearance of a 3'-biotinylated, internally [32P]-labeled phosphodiester oligodeoxynucleotide coupled to a neutral avidin/monoclonal antibody conjugate.

Provides evidence that at the time of filing that the conjugation of polynucleotides to proteins, and delivery of said compositions was being tested *in vivo*.

Conclusion

No claim is allowed.

As indicated previously, the claims are free of the art of record because the art fails to teach compounds with the structural and functional properties of those instantly claimed. However, the claims are subject other rejections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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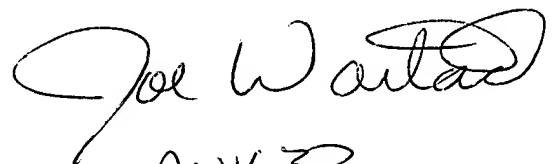
however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach


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